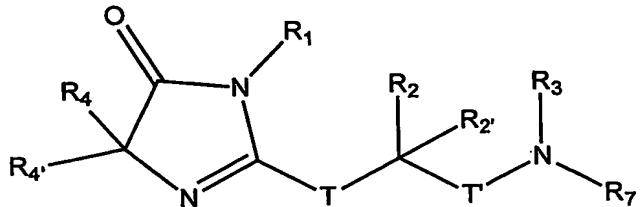


What is claimed is:

1. A compound selected from the group represented by Formula I:



Formula I

wherein:

T and T' are independently a covalent bond or optionally substituted lower alkylene;

R₁ is hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, or optionally substituted heteroaralkyl-;

R₂ and R_{2'} are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl; or R₂ and R_{2'} taken together form an optionally substituted 3- to 7-membered ring which optionally incorporates from one to two heteroatoms, selected from N, O, and S in the ring;

R₃ is hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, -C(O)-R₆, or -S(O)₂-R_{6a};

R₄ and R_{4'} are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; or R₄ and R_{4'}, together with the carbon to which they are attached form an optionally substituted 3- to 7-membered

ring which optionally incorporates from one to two heteroatoms, selected from N, O, and S in the ring; or R₄, taken together with R_{4'}, is an optionally substituted alkylidene;

R₆ is hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, R₉O- or R₁₁-NH-;

R_{6a} is optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, or R₁₁-NH-;

R₇ is hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

or R₇ taken together with R₃, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, chosen from N, O, and S in the heterocycle ring;

or R₇ taken together with R₂ form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, chosen from N, O, and S in the heterocycle ring;

R₉ is optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl; and

R₁₁ is hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

(Formula I including single stereoisomers and mixtures of stereoisomers);
a pharmaceutically acceptable salt of a compound of Formula I;
a pharmaceutically acceptable solvate of a compound of Formula I; or
a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I.

2. A compound of claim 1 comprising one or more of the following:
one of T and T' is a covalent bond and the other is a covalent bond or optionally substituted lower alkylene;
R₁ is optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;
R₂ is optionally substituted C₁-C₄ alkyl;
R_{2'} is hydrogen or optionally substituted C₁-C₄ alkyl;
R₃ is -C(O)R₆;
R₄ and R_{4'} are independently chosen from hydrogen, optionally substituted aryl and optionally substituted aryl-C₁-C₄-alkyl-;
R₆ is optionally substituted C₁-C₈ alkyl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heteroaryl-C₁-C₄-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R₁₁O- or R₁₂-NH-;
R₁₁ is optionally substituted C₁-C₈ alkyl or optionally substituted aryl;
R₁₂ is hydrogen, optionally substituted C₁-C₈ alkyl or optionally substituted aryl; and
R₇ is hydrogen, optionally substituted C₁-C₁₃ alkyl, optionally substituted aryl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heterocyclyl, or optionally substituted heteroaryl-C₁-C₄-alkyl-.
3. A compound of claim 1 comprising one or more of the following:
one of T and T' is a covalent bond and the other is a covalent bond or optionally substituted lower alkylene;
R₁ is optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;
R₂ is optionally substituted C₁-C₄ alkyl;
R_{2'} is hydrogen or optionally substituted C₁-C₄ alkyl;
R₃ is -C(O)R₆;
R₄ and R_{4'}, together with the carbon to which they are attached form an optionally

substituted 3- to 7-membered ring which optionally incorporates from one to two heteroatoms, selected from N, O, and S in the ring;

R₆ is optionally substituted C₁-C₈ alkyl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heteroaryl-C₁-C₄-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R₁₁O- or R₁₂-NH-;

R₁₁ is optionally substituted C₁-C₈ alkyl or optionally substituted aryl;

R₁₂ is hydrogen, optionally substituted C₁-C₈ alkyl or optionally substituted aryl; and

R₇ is hydrogen, optionally substituted C₁-C₁₃ alkyl, optionally substituted aryl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heterocyclyl, or optionally substituted heteroaryl-C₁-C₄-alkyl-.

4. A compound of claim 1 comprising one or more of the following:

one of T and T' is a covalent bond and the other is a covalent bond or optionally substituted lower alkylene;

R₁ is optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂' is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ is -C(O)R₆;

R₄, taken together with R_{4'}, is an optionally substituted alkylidene;

R₆ is optionally substituted C₁-C₈ alkyl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heteroaryl-C₁-C₄-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R₁₁O- or R₁₂-NH-;

R₁₁ is optionally substituted C₁-C₈ alkyl or optionally substituted aryl;

R₁₂ is hydrogen, optionally substituted C₁-C₈ alkyl or optionally substituted aryl; and

R₇ is hydrogen, optionally substituted C₁-C₁₃ alkyl, optionally substituted aryl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heterocyclyl, or optionally substituted heteroaryl-C₁-C₄-alkyl-.

5. A compound of claim 2, 3, or 4 comprising one or more of the following:
- T and T' are each a covalent bond;
- R₁ is ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, or (ethoxycarbonyl)ethyl;
- R₂ is methyl, ethyl, propyl, butyl, methylthioethyl, methylthiomethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, or hydroxymethyl;
- R₂ is hydrogen;
- R₆ is optionally substituted C₁-C₈ alkyl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heteroaryl-C₁-C₄-alkyl-, optionally substituted heteroaryl, or optionally substituted aryl; and
- R₇ is hydrogen, C₁-C₄ alkyl; cyclohexyl; phenyl substituted with hydroxyl, C₁-C₄ alkoxy or C₁-C₄ alkyl; benzyl; or R₁₆-alkylene-, wherein R₁₆ is hydroxyl, carboxy, (C₁-C₄ alkoxy)carbonyl-, di(C₁-C₄ alkyl)amino-, (C₁-C₄ alkyl)amino-, amino, (C₁-C₄ alkoxy)carbonylamino-, C₁-C₄ alkoxy-, or optionally substituted N-heterocyclyl-.
6. A compound of claim 5 comprising one or more of the following:
- R₁ is ethyl, propyl, methoxyethyl, naphthyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, or (ethoxycarbonyl)ethyl;
- R₂ is ethyl or propyl;
- R₆ is optionally substituted phenyl; and
- R₇ is R₁₆-alkylene-, wherein R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl.

7. A compound of claim 6 comprising one or more of the following:

R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R₂ is i-propyl; and

R₆ is toyl, halophenyl, methylhalophenyl, hydroxymethyl-phenyl, halo(trifluoromethyl)phenyl-, methylenedioxyphenyl, formylphenyl or cyanophenyl; R₇ is aminoethyl, aminopropyl, aminobutyl, aminopentyl, aminohexyl, methylaminoethyl, methylaminopropyl, methylaminobutyl, methylaminopentyl, methylaminohexyl, dimethylaminoethyl, dimethylaminopropyl, dimethylaminobutyl, dimethylaminopentyl, dimethylaminohexyl, ethylaminoethyl, ethylaminopropyl, ethylaminobutyl, ethylaminopentyl, ethylaminohexyl, diethylaminoethyl, diethylaminopropyl, diethylaminobutyl, diethylaminopentyl, or diethylaminohexyl.

8. A compound of claim 7 wherein R₁ is benzyl.

9. A compound of claim 1 comprising one or more of the following:

one of T and T' is a covalent bond and the other is a covalent bond or optionally substituted lower alkylene;

R₁ is optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂ is hydrogen or optionally substituted C₁-C₄ alkyl;

R₄ and R_{4'} are independently chosen from hydrogen, optionally substituted aryl and optionally substituted aryl-C₁-C₄-alkyl-; and

R₇ taken together with R₃, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, chosen from N, O, and S in the heterocycle ring.

10. A compound of claim 1 comprising one or more of the following:

one of T and T' is a covalent bond and the other is a covalent bond or optionally substituted lower alkylene;

R₁ is optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂' is hydrogen or optionally substituted C₁-C₄ alkyl;

R₄ and R_{4'}, together with the carbon to which they are attached form an optionally substituted 3- to 7-membered ring which optionally incorporates from one to two heteroatoms, selected from N, O, and S in the ring; and

R₇ taken together with R₃, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, chosen from N, O, and S in the heterocycle ring.

11. A compound of claim 1 comprising one or more of the following:

one of T and T' is a covalent bond and the other is a covalent bond or optionally substituted lower alkylene;

R₁ is optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂' is hydrogen or optionally substituted C₁-C₄ alkyl;

R₄, taken together with R_{4'}, is an optionally substituted alkylidene; and

R₇ taken together with R₃, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, chosen from N, O, and S in the heterocycle ring.

12. A compound of claim 9, 10, or 11 comprising one or more of the following:

T and T' are each a covalent bond;

R₁ is ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl,

chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, or (ethoxycarbonyl)ethyl;

R₂ is methyl, ethyl, propyl, butyl, methylthioethyl, methylthiomethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, or hydroxymethyl;

R₂ is hydrogen; and

R₃ taken together with R₇ and the nitrogen to which they are bound, forms an optionally substituted imidazolyl ring.

13. A compound of claim 9, 10, or 11 comprising one or more of the following:

T and T' are each a covalent bond;

R₁ is ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, or (ethoxycarbonyl)ethyl;

R₂ is methyl, ethyl, propyl, butyl, methylthioethyl, methylthiomethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, or hydroxymethyl;

R₂ is hydrogen; and

R₃ taken together with R₇, and the nitrogen to which they are bound, forms an optionally substituted imidazolinyl ring.

14. A compound of claim 9, 10, or 11 comprising one or more of the following:

T and T' are each a covalent bond;

R₁ is ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl,

methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, or (ethoxycarbonyl)ethyl;

R₂ is methyl, ethyl, propyl, butyl, methylthioethyl, methylthiomethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, or hydroxymethyl;

R₂ is hydrogen; and

R₃ taken together with R₇ forms an optionally substituted piperazine- or diazepam ring.

15. A compound of claim 9, 10, or 11 comprising one or more of the following:

R₁ is ethyl, propyl, methoxyethyl, naphthyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, or (ethoxycarbonyl)ethyl;

R₂ is methyl, ethyl, propyl, butyl, methylthioethyl, methylthiomethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, or hydroxymethyl; and

R₂ is hydrogen.

16. A compound of claim 15 comprising one or more of the following:

R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl; and

R₂ is ethyl or propyl.

17. A compound of claim 16 comprising one or more of the following:

R₁ is benzyl; and

R₂ is i-propyl.

18. A compound of claim 1 wherein

T and T' are each a covalent bond;

R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or

hydroxybenzyl;

R₂ is hydrogen;

R₂ is optionally substituted C₁-C₄ alkyl;

R₄ and R_{4'} are independently chosen from hydrogen, optionally substituted aryl and optionally substituted aryl-C₁-C₄-alkyl;

R₃ is -C(O)R₆;

R₆ is optionally substituted phenyl; and

R₇ is R₁₆-alkylene-, wherein R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl.

19. A compound of claim 1 wherein

T and T' are each a covalent bond;

R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R₂' is hydrogen;

R₂ is optionally substituted C₁-C₄ alkyl;

R₄ and R_{4'}, together with the carbon to which they are attached form an optionally substituted 3- to 7-membered ring which optionally incorporates from one to two heteroatoms, selected from N, O, and S in the ring;

R₃ is -C(O)R₆;

R₆ is optionally substituted phenyl; and

R₇ is R₁₆-alkylene-, wherein R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl.

20. A compound of claim 1 wherein

T and T' are each a covalent bond;

R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R₂' is hydrogen;

R₂ is optionally substituted C₁-C₄ alkyl;

R₄, taken together with R_{4'}, is an optionally substituted alkylidene;
R₃ is -C(O)R₆;
R₆ is optionally substituted phenyl; and
R₇ is R₁₆-alkylene-, wherein R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl.

21. A compound of claim 1 wherein
T and T' are each a covalent bond;
R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;
R₂ is hydrogen;
R₂ is optionally substituted C₁-C₄ alkyl;
R₄ and R_{4'} are independently chosen from hydrogen, optionally substituted aryl and optionally substituted aryl-C₁-C₄-alkyl; and
R₃ taken together with R₇, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

22. A compound of claim 1 wherein
T and T' are each a covalent bond;
R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;
R₂ is hydrogen;
R₂ is optionally substituted C₁-C₄ alkyl;
R₄ and R_{4'}, together with the carbon to which they are attached form an optionally substituted 3- to 7-membered ring which optionally incorporates from one to two heteroatoms, selected from N, O, and S in the ring; and
R₃ taken together with R₇, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which

optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

23. A compound of claim 1 wherein
T and T' are each a covalent bond;
R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;
R₂ is hydrogen;
R₂ is optionally substituted C₁-C₄ alkyl;
R₄, taken together with R_{4'}, is an optionally substituted alkylidene;
R₃ taken together with R₇, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.
24. A compound of claim 1 that is
N-(3-Amino-propyl)-N-[1-(6-benzyl-7-oxo-4,6-diaza-spiro[2.4]hept-4-en-5-yl)-2-methyl-propyl]-4-methyl-benzamide; or
N-(3-Amino-propyl)-N-[1-(1-benzyl-4-isopropylidene-5-oxo-4,5-dihydro-1H-imidazol-2-yl)-2-methyl-propyl]-4-methyl-benzamide, or
a pharmaceutically acceptable salt, solvate or solvate of a salt thereof.
25. A compound of any of the above claims wherein the stereogenic center to which R₂ and R_{2'} is attached is of the R configuration.
26. A composition comprising a pharmaceutical excipient and a compound of any one of claims 1-24.
27. A composition according to claim 26, wherein said composition further comprises a chemotherapeutic agent other than a compound of claim 1.

28. A composition according to claim 27 wherein said chemotherapeutic agent is a taxane, a vinca alkaloid, or a topoisomerase I inhibitor.
29. A method of modulating KSP kinesin activity which comprises contacting said kinesin with an effective amount of a compound according to any one of claims 1 to 24.
30. A method of inhibiting KSP which comprises contacting said kinesin with an effective amount of a compound according to any one of claims 1 to 24.
31. A method for the treatment of a cellular proliferative disease comprising administering to a patient in need thereof a compound according to any one of claims 1-24.
32. A method for the treatment of a cellular proliferative disease comprising administering to a patient in need thereof a composition according to any one of claims 26-28.
33. A method according to claim 31 or claim 32 wherein said disease is selected from cancer, hyperplasias, restenosis, cardiac hypertrophy, immune disorders, and inflammation.
34. The use, in the manufacture of a medicament for treating cellular proliferative disease, of a compound according to any one of claims 1-24.
35. The use of a compound as defined in claim 34 for the manufacture of a medicament for treating a disorder associated with KSP kinesin activity.